

We Claim:

1. A device for detecting Raman spectroscopic signals, comprising:
  - a substrate having an enhancing surface thereon;
  - 5 a passivating agent associated with said enhancing surface; and
  - an analyte receptor associated with said enhancing surface.
2. The device of claim 1, wherein said enhancing surface comprises fractal aggregates.
- 10 3. The device of claim 1, wherein said enhancing surface comprises a metal.
4. The device of claim 1, wherein said passivating agent decreases direct association of an analyte with said enhancing surface.
- 15 5. The device of claim 1, wherein the degree of passivation results in a decrease in a Raman signal of an analyte associated with said enhancing surface by at least 50% after 20 washing steps.
- 20 6. The device of claim 1, wherein the degree of passivation results in a decrease in a Raman signal of an analyte associated with said enhancing surface by greater than about 50% with one washing step.
7. The device of claim 1, wherein the degree of passivation results in a decrease in a Raman signal of an analyte associated with said enhancing surface by greater than about 95% with one washing step.
- 25 8. The device of claim 1, wherein said substrate is glass.
- 30 9. The device of claim 1, wherein said substrate is quartz.

10. The device of claim 3, wherein said metal layer is gold.
11. The device of claim 3, wherein said metal layer is aluminum.
- 5 12. The device of claim 2, wherein said fractal aggregates comprise gold.
13. The device of claim 2, wherein said fractal aggregates comprise silver.
14. The device of claim 1, wherein said passivating agent is selected from the  
10 group consisting of 2-mercaptoethanol, ethanedithiol, mercaptoethylamine, cysteine  
and cystine.
- 15 15. The device of claim 1, wherein said analyte receptor is associated with a  
polymer on said substrate.
16. The device of claim 1, wherein said analyte receptor comprises an antigen.
17. The device of claim 16, wherein said analyte comprises an antibody against  
said antigen.
- 20 18. The device of claim 16, wherein said antigen comprises DNP.
19. The device of claim 17, wherein said antibody is an anti- DNP antibody.
- 25 20. The device of claim 1, wherein said analyte receptor is selected from the group  
consisting of acetylcysteine, mercaptosuccinic acid and mercaptopurine, purine,  
polyoxyethylenes, crown ethers, cryptates, polyoxyethylenes in which NH replaces at  
least one oxygen atom, molecules containing NH<sub>2</sub>, C(O)OH, SH, CN, OH, C(O)NH<sub>2</sub>,  
C(O)Cl, disulfide groups, glutathione, mercaptosuccinic acid, mercaptopurine, purine,  
30 uracil, and NADP.

21. The device of claim 1, wherein said analyte receptor comprises a hydrophobic molecule.
22. The device of claim 1, wherein said analyte receptor comprises a self-  
5 assembled monolayer comprising a member of the group consisting of alkylthiols and disulfides.
23. A biochip comprising:  
a substrate having a passivated enhancing surface thereon, said passivated  
10 surface having at least one defined area thereon;  
said defined area having a plurality of analyte receptors preferentially localized near enhancing surface.
24. The biochip of claim 23, wherein said enhancing surface comprises a fractal structure.  
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25. The biochip of claim 23, wherein said substrate is selected from the group consisting of silicon, silicon dioxide, glass, and plastics.
- 20 26. The biochip of claim 23, wherein said passivating agent is selected from the group consisting of 2-mercaptoethanol, ethanedithiol, mercaptoethylamine, cysteine and cystine.
27. The biochip of claim 23, wherein said analyte receptor comprises an antigen.  
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28. The biochip of claim 23, wherein said analyte receptor is selected from the group consisting of acetylcysteine, mercaptosuccinic acid and mercaptopurine, purine, polyoxyethylenes, crown ethers, cryptates, polyoxyethylenes in which NH replaces at least one oxygen atom, molecules containing NH<sub>2</sub>, C(O)OH, SH, CN, OH, C(O)NH<sub>2</sub>,  
30 C(O)Cl, disulfide groups, glutathione, mercaptosuccinic acid, uracil, and NADP.

29. The biochip of claim 27, wherein said analyte comprises an antibody directed against said antigen.

30. A method for passivating a surface for Raman spectroscopy, comprising the  
5 steps of:

- providing a substrate having an enhancing surface thereon;;
- applying a passivating agent to said enhancing surface; and
- permitting said passivating agent to associate with said enhancing surface.

10 31. The method of claim 30, wherein said enhancing surface comprises fractal aggregates.

32. The method of claim 30, wherein said enhancing surface comprises a metal layer.

15 33. The method of claim 32, wherein said metal layer comprises gold.

34. The method of claim 30, wherein said metal comprises aluminum.

20 35. The method of claim 30, wherein said metal comprises aluminum.

36. A method for detecting an analyte, comprising the steps of:

(a) providing a substrate having a passivated enhancing surface and analyte receptors thereon;

(b) contacting a solution containing an analyte which binds with said analyte receptor for sufficient time to permit binding of said analyte to said analyte receptor; and

(c) detecting by Raman spectroscopy, the presence of said analyte associated with said analyte receptor.

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37. A method for quantifying the amount of an analyte, comprising the steps of:

- (a) providing a substrate having a passivated enhancing surface and analyte receptors thereon;
- (b) contacting a solution containing an analyte which binds with said analyte receptor for sufficient time to permit sufficient binding of said analyte to said analyte receptor to allow detection of a Raman spectral feature associated with said analyte;
- 5 (c) detecting said Raman spectral feature; and
- (e) comparing said spectral feature of said analyte with a calibration curve for said analyte.

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38. A kit for quantitative Raman spectroscopy, comprising:
- a substrate having at least one passivated enhancing surface and analyte receptors thereon; and
- an analyte standard for calibration.

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39. A kit for quantitative Raman spectroscopy, comprising:
- a substrate having at least one passivated enhancing surface and analyte receptors thereon;
- an analyte standard for calibration; and

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a Raman spectrometer.

40. A device for measuring an analyte, comprising:
- a flow-through cell having a passivated enhancing surface with at least one analyte receptor thereon;
- a window in said flow-through cell that permits electromagnetic radiation to pass;
- means for causing fluid to flow through a chamber of said flow-through cell; and
- a Raman detector associated with said window.

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41. The flow-through cell of claim 40, further comprising a second fluid chamber

attached to said first fluid chamber.

42. The device of claim 1, wherein said analyte receptor is associated with said enhancing surface by a polymer.

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43. The device of claim 42, wherein said polymer comprises between about 6 and about 10,000,000 monomers.

44. The device of claim 42, wherein said polymer is selected from the group  
10 consisting of dithiobis(succinimidyl propionate), dimethyl 3,3'-  
dithiobispropionimide •2HCl, and 3,3'-dithiobis(sulfosuccinimidyl propionate),

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